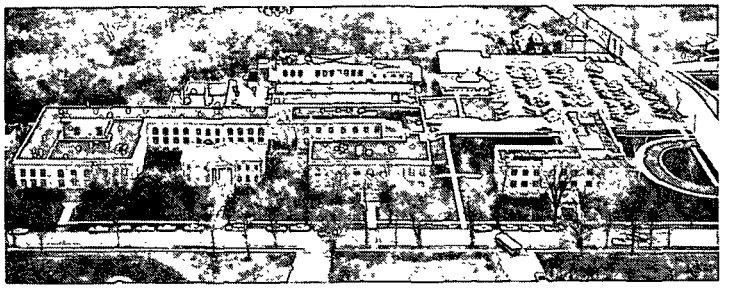

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INSOLUBLE LIGNIN MODELS (1): SYNTHESIS OF LIGNIN DIMERS CONTAINING PROPYL ALCOHOL APPENDAGES

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INSOLUBLE LIGNIN MODELS (1): SYNTHESIS OF LIGNIN DIMERS CONTAINING PROPYL ALCOHOL APPENDAGES

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ABSTRACT

Three lignin model dimers have been synthesized. The models contain propyl alcohol appendages on C5 of ring A (12), C4 of ring B (15), and Cβ of the side chain (21), respectively. The propyl alcohol appendages will serve as "handles" for bonding the models to a polymer matrix. Model 21 has also been used to diagnostically examine the delignification efficiences of pulping chemicals.

INTRODUCTION

Its random, crosslinked, polymeric structure[1] makes studying reactions of lignin difficult, primarily because the starting material cannot be well characterized and there are a multitude of products formed. Consequently, researchers have resorted to studying reactions of well-defined lignin models.[2-5] The models generally are patterned after a lignin dimer unit which is believed to be present in the polymer. However, these models are generally water soluble and their reactions may not accurately reflect the chemistry occurring with water insoluble lignin materials. Therefore, we have begun studying the synthesis and reactions of heterogeneous (insoluble) lignin models.

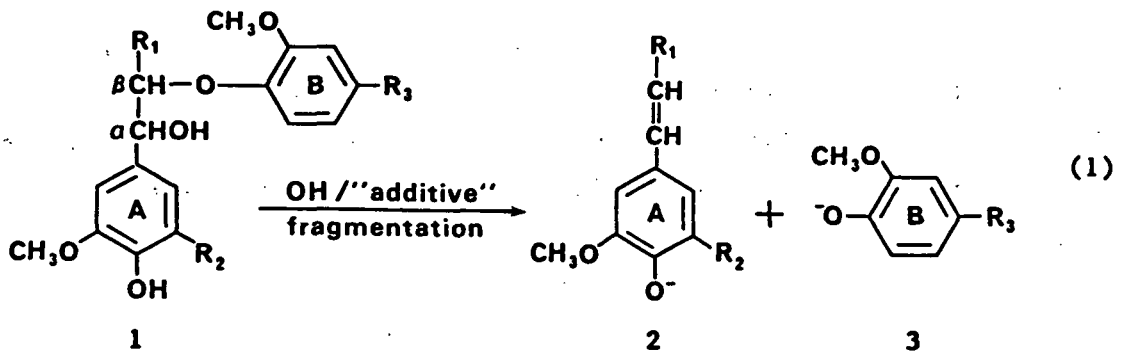
This report describes the synthesis of three lignin model dimers which have propyl alcohol appendages ("handles"). The primary

alcohol handle will provide the site of bonding to the polymer.[5] The precedence for polymer binding to a primary alcohol, in the presence of other hydroxyl groups, is provided in several synthetic carbohydrate studies. For example, monosaccharides can be bound to polymers at the C_6-primary alcohol groups with triphenylmethyl (trityl) linkages,[6] selective reactions can then be performed on secondary hydroxyl groups of the immobilized carbohydrates, and the modified carbohydrates can be released from the polymers by acid treatment.[7,8] Similar reactions should be possible for a lignin model compound.[9,10]

The principal considerations which need to be addressed when designing a model with a primary alcohol handle are (1) the model type, (2) the location of the handle, and (3) the length of the handle. The most desirable model is a β-aryl ether type. A large number of mechanistic studies have been done with this model type, and direct comparison of homogeneous vs. heterogeneous reactions would be very informative.

The length of the primary alcohol handle was chosen to be three carbons (propyl) because of the ease of synthesis and to provide sufficient distance between the reactive parts of the model and the bonding site. Reasonable distances are needed to ensure that steric inhibition to reaction is not a factor.

The location of the handle (and thus the polymer linkage) plays a role in product analysis. Equation 1 illustrates a typical lignin model fragmentation reaction. The extent of fragmentation is generally determined by the amount of simple phenol 3



released and not the amount of the styrene product 2.[11] The latter is prone to polymerize; consequently, its observed yields are often low and do not accurately reflect the amount of reaction.

A polymer attachment through ring B (i.e., 1, R_3-attachment) would liberate upon fragmentation a styrene product into the solution phase which may be difficult to quantitate accurately. A better attachment would be through ring A (i.e., 1, R_2-attachment) or the side chain (i.e., 1, R_1-attachment) so that fragmentation would liberate into solution an easily-analyzable phenol (3). We describe here the synthesis of three models in which there is a propyl alcohol "handle" on the ring A, ring B, and C_β positions, respectively.

RESULTS AND DISCUSSION

A-Ring Handle Model

We sought a "generic" procedure, one which would start with any of a variety of already conventional lignin dimers and add a propyl alcohol handle to it. Portions of a recently described coumarin synthesis appeared suitable. Panetta and Rapoport[12] report that 2,2-diethoxychroman is formed when guaiacol is reacted with triethylorthoacrylate. We have found that a diethoxychroman can also be prepared from a <u>para</u>-acyl phenol and can be converted into a propyl alcohol handle (Fig. 1).

Placing a propyl handle on the A-ring was first attempted with the readily available acetoguaiacone (4). The diethoxychroman 6 was formed in excellent yield (ca. 74%) and was subsequently hydrolyzed with HCl to give the ester 7. The simultaneous reduction of the α-carbonyl and ethyl ester of 7 was effected with $LiAlH_4$, giving compound 8, a lignin model monomer with a primary alcohol handle.

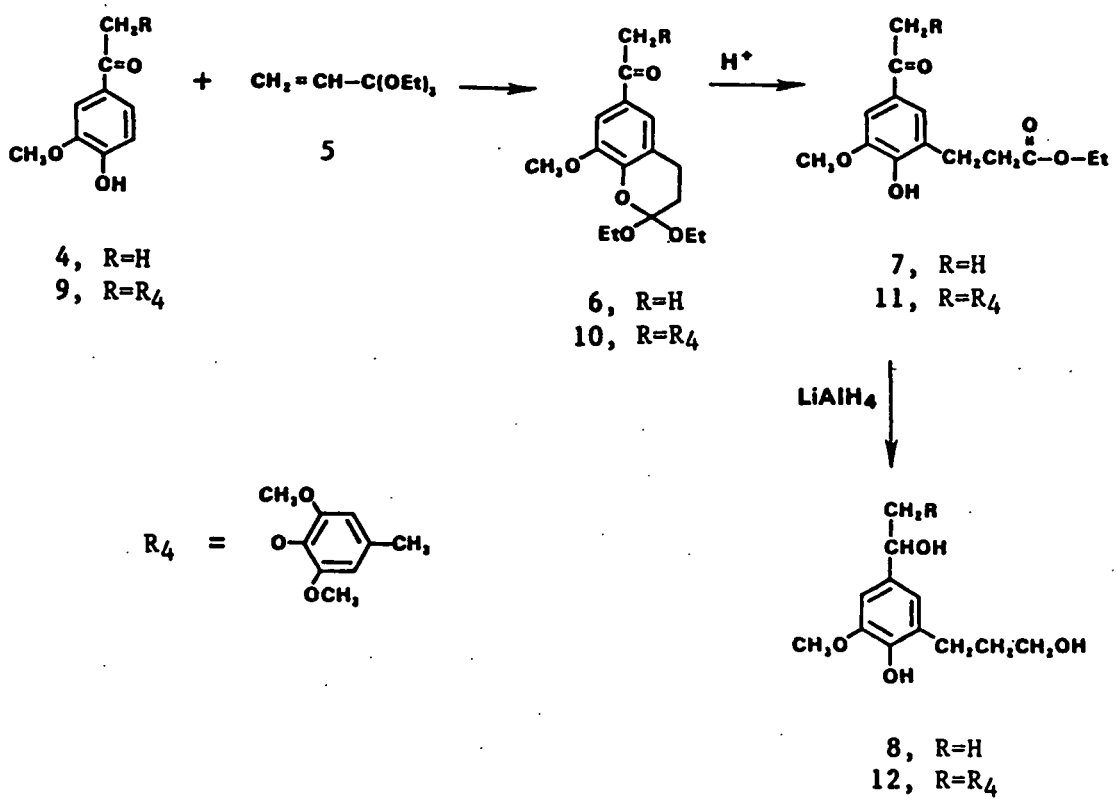


Figure 1. Adaptation of Panetta and Rapoport's[12] coumarin synthesis for the introduction of a propyl alcohol handle to acetoguaiacone (4) and lignin dimer 9.

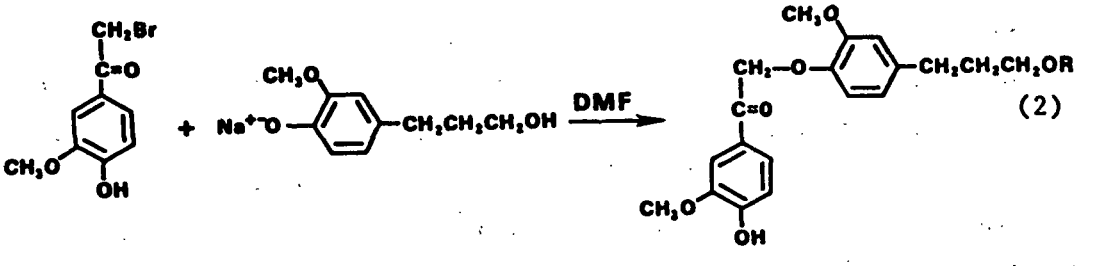
Similarly, the phenacyl β-aryl ether 9 was subjected to the identical synthetic sequence. (Conventional lignin model 9 can be prepared by several techniques.[13,14]) The desired compound 12 was successfully prepared in an overall yield of 58% (3-steps, from 9). This synthetic sequence should be applicable for introducing a primary alcohol handle to a variety of other lignin dimers with different β-aryl groups and/or β-alkyl substituents. However, problems in derivatizing[5] the A-ring propanol model 10 led us to seek alternative functionalized models.

B-Ring Handle Model

As mentioned previously, the alkaline fragmentation of a polymer-bound model based on B-ring attachment would liberate a styrene product which may be difficult to analyze quantitatively. Alternatively, a B-ring handle model which has an α-carbonyl rather

than an α-hydroxyl could be a useful model; the alkaline degradation of phenacyl aryl ethers has been studied.[15] The alkaline fragmentation of 15 bound to a polymer at the propyl alcohol site should liberate acetoguaiacone (4), a product which should be easily quantified.

Ketone 15 was obtained in roughly 60% yield from the coupling of β-bromoketone 13[13] with the sodium salt of 3-(3-methoxy-4-hydroxyphenyl)-1-propanol (14) [Eq. (2)]. The latter was prepared by (a) hydrogenation of ferulic acid over palladium on carbon, (b) reduction of the resulting dihydroferulic acid with borane-THF or $LiAlH_4$, and (c) treating with NaOH. Compound 15 was tritylated in a modest 35% yield (after chromatography) with trityl pyridinium tetrafluoroborate[16] to give 15-Tr. This latter reaction demonstrated that the propyl OH can be selectively functionalized in the presence of a phenolic OH group and that 15 could possibly be bound to a polymer <u>via</u> a trityl ether linkage.

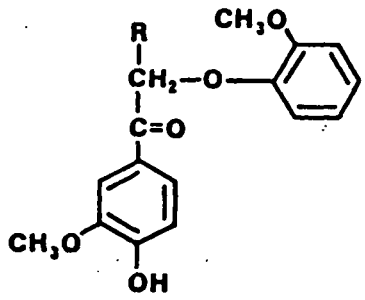


(2)

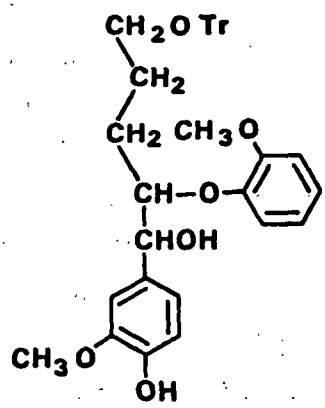
13 14-Na salt 15, R=H
15-Tr, R=CPh_3

Beta-Position Handle Model

One way to functionalize the side chain of a lignin model is alkylation of the β-carbon of an α-keto structure. For example, 16 can be alkylated with methyl iodide or formaldehyde to give 17 or 18, respectively; however, the alkylation failed with ethyl, propyl, and benzyl halides.[17] We were gratified to find that 16 was alkylated with allyl bromide to give ketone 19 in 68% yield. Apparently, a highly reactive substrate, such as allyl bromide,[18] is needed for a successful alkylation of ketone 16.



16, R=H
17, R=CH_3
18, R=CH_2OH
19, R=$CH_2CH{=}CH_2$



21-Tr

The β-allyl ketone 19 was transformed to the desired β-propanol alcohol 21 in two ways. The two routes (Fig. 2) differ in the order in which following steps were performed: (1) hydroboration of terminal olefin with disiamylborane (DSB) followed by an oxidative work-up with hydrogen peroxide (O)[19] to give a terminal alcohol and (2) sodium borohydride reduction of the α-carbonyl group to a benzyl alcohol. Either route involves the introduction of a second asymmetric carbon (step A_2 or B_1) and the likelihood of producing mixtures of erythro/threo diastereomers.

Route A afforded a mixture of diastereomers of 21 which could not be separated by chromatography techniques. Route B, on the other hand, gave a mixture of isomers after the first step, which could be chromatographically separated; hydroboration of the major isomer of alcohol 22 afforded one diastereomer of 21 as a crystalline product. Both routes gave the same diastereomer as the major product. The yield of the three-step conversion of 16 to 21 was 28% (roughly 66% for each step).

The $NaBH_4$ reduction steps on either ketone 19 (step B_1) or ketone 20 (step A_2) might be expected to show a preference for one diastereomer product over the other, since the carbon adjacent to

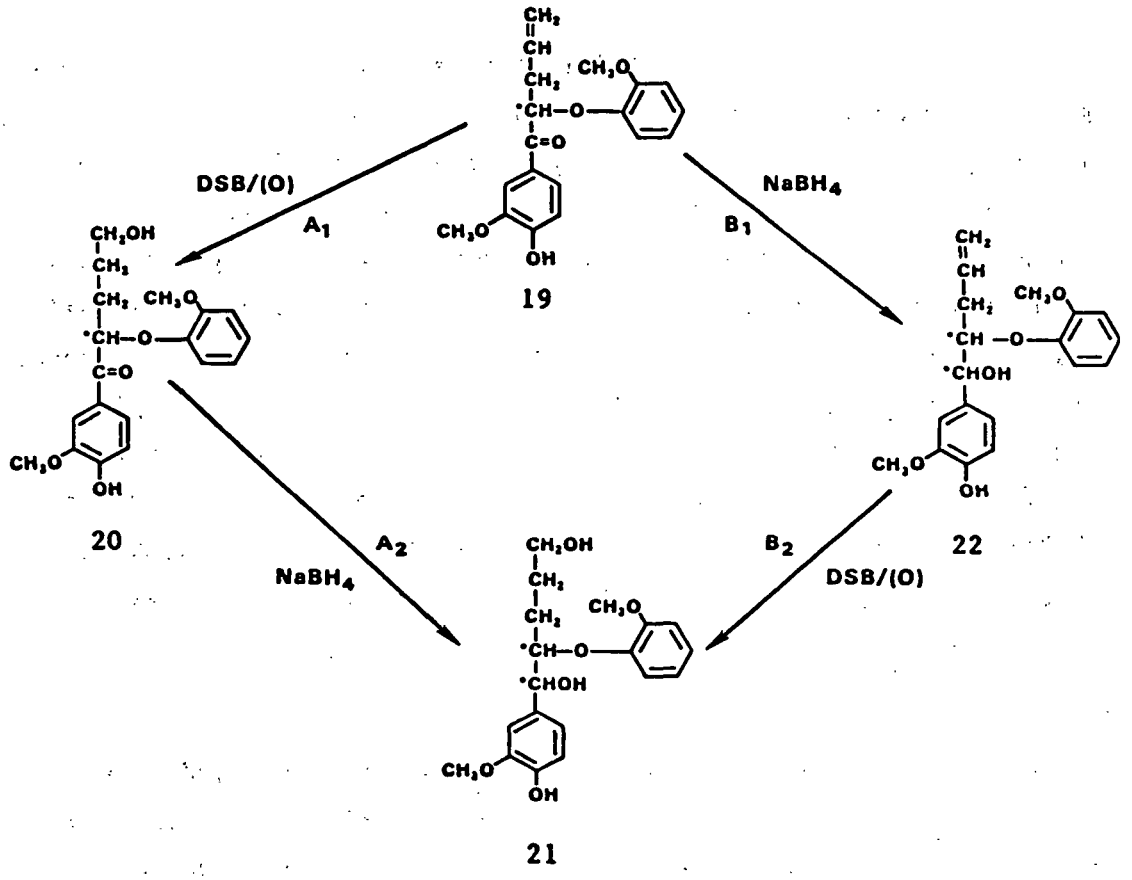


Figure 2. Two routes (A and B) used to reduce the α-carbonyl group and convert the allyl substituent to a propanol substituent.

the carbonyl group under reduction is asymmetric.[20] Steric differences in the substituents on the asymmetric carbon can sometimes produce high selectivities for a particular diastereomer product.[21,22] In our case, there are neighboring ether oxygens and hydroxyl groups which might also direct the attack of $NaBH_4$ species on the carbonyl group; accurate prediction of the stereochemistry of the major isomer of 21 formed may be difficult.

The fact that the propyl alcohol handle can be functionalized selectively in the presence of secondary benzyl OH group and phenolic OH group was demonstrated by treating 21 with trityl chloride/pyridine and observing the production of a primary trityloxy product, 21-Tr, in 64% yield. Such a result suggests that 21 could be bound to a polymer <u>via</u> a trityl ether linkage.[5]

SUMMARY

Three unique lignin model dimers have been prepared. Each new model is similar to lignin models which have been routinely studied, but unique in that they all incorporate a propyl alcohol handle onto their respective dimer, each at a different position. The synthetic routes leading to β-aryl ethers 12 and 21 might possibly be used to introduce a propyl alcohol handle to a variety of available lignin models. The third synthesis, leading to a B-ring handle model is specific in that it does not involve adding a propyl alcohol side-chain to an already prepared lignin model dimer.

Studies on the degradation reactions of models 21, 21-Tr, and 22 have provided interesting data on the efficiency by which pulping chemicals (HO^-, HS^-, and AHQ^{-2}) fragment these models.[24]

EXPERIMENTAL

General Information - Proton and ^{13}C-NMR were recorded on a Jeol FX-100 spectrometer using $CDCl_3$ or d_6-DMSO as a solvent and TMS as an internal reference. Infrared spectra were recorded on a Perkin-Elmer Model 700 infrared spectrometer and standardized with polystyrene. Electron impact mass spectra were obtained at 70 eV using a direct insertion probe (DIP) with a Hewlett-Packaged 5985 mass spectrometer. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

All solvents employed, unless indicated otherwise, were A.C.S. reagent grade. Reagents and starting materials were obtained from Aldrich Chemical Co., Milwaukee, Wisconsin. All melting points recorded are uncorrected.

4-Hydroxy-3-methoxy-β-(2,6-dimethoxy-4-methylphenoxy)acetophenone (9) - The phenacyl β-aryl ether 9 was prepared according to the general method of Miksche;[14] its specific preparation is detailed elsewhere.[24]

6-Acetyl-2,2-diethoxy-8-methoxychroman (6) - Into 150 mL of toluene was dissolved 15.0 g (90.4 mmol) of acetoguaiacone (4),

9.2 g (90.4 mmol) of pivalic acid, and 31.5 g (180.8 mmol) of triethylorthoacrylate (5).[25] The mixture was refluxed for 24 hr, cooled, diluted with 30 mL of ether, washed with 1N NaOH, water, and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo to give a gold oil which crystallized upon standing. (Acidification and ether extraction of the NaOH resulted in the recovery of ca. 0.9 g of starting material.) Recrystallization of the gold solid from hexane gave 19.8 g (74.2%) of light yellow crystals of 6: mp 81.0-84.0°C; IR (mull) cm^{-1} 1680 (C=O); ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, J = 7 Hz, 6, OCH_2CH_3), 2.12 (t, J = 7 Hz, 2, $ArCH_2CH_2$), 2.55 (s, 3, $COCH_3$), 2.91 (t, J = 7 Hz, 2, $ArCH_2$), 3.72 (q, J = 7 Hz, 2, OCH_2CH_3), 3.74 (q, J = 7 Hz, 2, OCH_2CH_3), 3.85 (s, 3, OCH_3), and 7.35 (s, 2, aryl).

Ethyl 5-acetyl-2-hydroxy-3-methoxydihydrocinnamate (7) - Into 200 mL of ether was dissolved 12.0 g (40.5 mmol) of 6. To this mixture was added 200 mL of 10% aqueous HCl and the two phase mixture was stirred for 2.25 hr. The phases were separated and the aqueous layer extracted with ether. The combined organic layers were washed with water and saturated aqueous NaCl, dried (Na_2SO_4), and evaporated to give 11.5 g of an oil which hardened upon standing to orange-gold crystals of 7: mp 64.0-65.0°C; IR (mull) cm^{-1} 3350 (OH), 1730 (ester C=O), 1670 (ketone C=O), and 1600 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3, CH_2CH_3), 2.54 (s, 3, $ArCOCH_3$), 2.67 (t, 2, $ArCH_2$), 3.08 (t, 2, $ArCH_2CH_2$), 3.92 (s, 3, OCH_3), 4.13 (q, 2, J = 7 Hz, $COOCH_2CH_3$), 6.59 (s, 1, OH), and 7.43 (s, 2, aryl).

1-(3-Methoxy-4-hydroxy-5-[γ-hydroxypropyl]phenyl) ethanol (8) - A slurry of 0.86 g (22.7 mmol) of $LiAlH_4$ in 35 mL of dry, freshly distilled THF was stirred while a solution of 2.0 g (8.8 mmol) of 7 in 35 mL THF was dripped in over 1 hr. The mixture was brought to and kept at reflux for 1.5 hr and then allowed to come to room temperature with stirring overnight. The reaction was quenched by the addition of saturated aqueous Na_2SO_4, until effervescing stopped and a nearly colorless granular solid was obtained. The

mixture was filtered and the collected residue rinsed with dry ether. The organic filtrate was reduced in vacuo to give 0.5 g of 8 as an oil: IR (neat) cm^{-1} 3350 (broad, OH), no carbonyl absorbances, and 1600 (aryl); ^{1}H-NMR (d_6-DMSO) δ 1.28 (d, J = 6 Hz, 3, CH_3), 1.64 (m, 2, $ArCH_2CH_2$), 2.53 (t, J = 8 Hz, 2, $ArCH_2$), 3.40 (t, J = 7 Hz, 2, CH_2OH), 3.76 (s, 3, OCH_3), 4.58 (q, J = 6.5 Hz, 1, ArCHOH), 5.38 (broad s, 3, three OH), 6.64 (s, 1, aryl), and 6.75 (s, 1, aryl).

The solid (aluminum salts) residue from above was dissolved in 1N H_2SO_4, and the acidic mixture was extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4), and reduced in vacuo to give ca. 0.3 g of an oil with spectra identical to the product 8 described above.

6-(2,6-Dimethoxy-4-methylphenoxyl)acetyl-2,2-diethoxy-8-methoxychroman (10) - Compound 9 was subjected to the identical procedure for preparing diethoxychromans (as described above) with the following quantities: 12.0 g (32.1 mmol) of 8, 1.64 g (6.05 mmol) of pivalic acid, and 11.2 g (64.2 mmol) of triethyl ortho-acrylate. The diethoxychroman 10, 17.5 g, was obtained as an oil and used without further purification: IR (neat) cm^{-1} 1690 (C=O), and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, J = 7 Hz, 6, CH_2CH_3), 2.11 (t, J = 7 Hz, 2, $ArCH_2CH_2$), 2.32 (s, 3, $ArCH_3$), 2.89 (t, J = 6.5 Hz, 2, $ArCH_2CH_2$), 3.44 (m, 4, OCH_2CH_3), 3.79 (s, 6, $ArOCH_3$), 3.88 (s, 3, $ArOCH_3$), 5.09 (s, 2, $ArCOCH_2$), 6.4 (s, 2, aryl), 7.22 (s, 1, aryl), and 7.50 (s, aryl).

Ethyl 5-(2,6-dimethoxy-4-methylphenoxyacetyl)-2-hydroxy-3-methoxydihydrocinnamate (11) - All of the crude product 10, from the previous procedure, was dissolved in 100 mL ether and stirred for 3 hr with 100 mL of 10% HCl. While the reaction proceeded, a fine white powder crystallized out of the ether phase. The entire reaction mixture was chilled; the white powder was collected on a fine porosity filter funnel and washed with cold water and ether to give 7.1 g of 11. The filtrate was separated and the ether layer washed with water and saturated aqueous NaCl, dried

(Na_2SO_4), and concentrated on a steam cone until slightly cloudy; upon cooling another 3.0 g of product was collected, to give a total of 10.1 g (72.7% two-step yield from 9) of 11: mp 111.5-113.0°C; IR (mull) cm^{-1} 3400 (OH), 1590 (aryl), 1660 (ketone C=O), and 1710 (ester C=O); ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3, CH_2CH_3), 2.32 (s, 3, $ArCH_3$), 2.64 (t, J = 6 Hz, 2, CH_2COO), 2.99 (t, J = 6 Hz, 2, CH_2CH_2COO), 3.80 (s, 6, $ArOCH_3$), 3.93 (s, 3, $ArOCH_3$), 4.11 (q, J = 7 Hz, 2, CH_2CH_3), 5.08 (s, 2, CH_2OAr), 6.40 (s, 3, two aryl-H and OH), and 7.21 (d, 2, aryl); ^{13}C-NMR ($CDCl_3$) ppm 14.2 (q, CH_2CH_3), 21.8 (q, $ArCH_3$), 25.4 (t, CH_2CH_2COO), 33.8 (t, CH_2COO), 55.9 (q, two $ArOCH_3$), 56.1 (q, $ArOCH_3$), 60.3 (CH_2CH_3), 75.1 (t, CH_2OAr), 105.8 (d, aryl C-3,5), 108.6 (d, aryl C-6), 124.0 (d, aryl C-2), 125.6, 126.9, 133.8, 133.9 (all d, aryl CH), 146.2, 148.3, 152.5 (all s, aryl C), 172.7 (s, COO), and 193.2 (s, ArCO); MS (DIP) m/e (%) 432 (16, M^+), 251 (38), 167 (100), and 77 (14).

1-(4-Hydroxy-3-methoxy-5-[γ-hydroxypropyl]phenyl)-2-(2,6-dimethoxy-4-methylphenoxyl)ethanol (12) - The $LiAlH_4$ reduction procedure used in the reduction of 7 was repeated with the following quantities and conditions: 5.0 g (11.6 mmol) of 11 and 1.2 g (32.4 mmol) of $LiAlH_4$; the mixture was refluxed for 21.5 hr. The reaction was quenched by the addition of saturated aqueous Na_2SO_4 giving a suspension of grey-white solid in the THF. The mixture was filtered and rinsed with copius quantities of ether. Additional product was recovered by rinsing the aluminum salts with CH_2Cl_2. The filtrates were washed with water and dried (Na_2SO_4) and concentrated in vacuo to give oils which were crystallized from ether to give a total of 3.7 g (82%) of 12: mp 110.0-111.0°C; IR (mull) cm^{-1} 3223, 3450 (OH), 1595 (aryl), and no C=O absorbances; ^{1}H-NMR (d_6-DMSO) (60°C) δ 1.69 (m, 2, $CH_2CH_2CH_2$), 2.25 (s, 3, $ArCH_3$), 2.56 (t, J = 7 Hz [with further fine splitting], 2, $ArCH_2$), 3.42 (t, J = 7 Hz, 2, CH_2OH), 3.6-4.1 (broad signal, 1, OH), 3.75, 3.77 (2 s, 6 + 3, $ArOCH_3$), 3.79 (d of d, J = 7.5 and 10 Hz, 1, CH_ACH_BOAr), 3.96 (d of d, J = 4.5 and 10 Hz, 1, CH_ACH_BOAr), 4.5-4.9 (broad signal, 1, OH), 4.71 (d of d, J = 4.5 and 7.5 Hz,

1, CHOH), 5.6-7.2 (broad signal, 1, OH), 6.47, 6.48 (2 s, 1 + 1, aryl), 6.70 (d, J = 2 Hz, 1, aryl), and 6.82 (d, J = 2 Hz, 1, aryl); ^{13}C-NMR (d_6-DMSO) ppm 21.3 (q, $ArCH_3$), 26.2 (t, $CH_2CH_2CH_2$), 32.8 (t, $ArCH_2$), 55.6 (q, $ArOCH_3$). 55.8 (q, two $ArOCH_3$), 60.5 (t, CH_2OH), 71.5 (d, CHOH), 78.5 (t, CH_2OAr), 106.3, 107.6, 119.7, 134.5 (all d, aryl CH), and 127.9, 131.9, 132.8, 142.9, 146.8, 152.3, (all s, aryl C); MS (DIP) m/e (%) 392 (2, M^+), 182 (5), 168 (100, $ArOH^+$), and 77 (5).

Anal. calcd. for $C_{21}H_{28}O_7$(%): C, 64.27; H, 7.19; O, 28.54. Found: C, 63.50; H, 7.17; O, 28.46.

3-(3-Methoxy-4-hydroxyphenyl)-1-propanol (14) - Into 700 mL of absolute ethanol was dissolved 50.0 g of ferulic acid, after which ca. 1.5 g of 10% Pd on carbon was added. The mixture was stirred while hydrogen was supplied to the reaction mixture from a balloon (attached to a 3-way stopcock), which could be periodically recharged with the gas; the reaction was allowed to proceed until no more hydrogen was consumed. The solution was filtered through CELITE, concentrated in vacuo to give a light brown oil, and crystallized from CH_2Cl_2/hexane to give 42.8 g (84.8%) of dihydroferulic acid as light-brown needles: mp 88.0-90.5°C (Lit.[26] 89-90°C).

Dihydroferulic acid, 40.0 g (20.4 mmol), was dissolved into 200 mL of dry, freshly distilled THF; all glassware was oven-dried and all operations, until the workup, were under dry nitrogen. To the dihydroferulic acid solution was added (in 5 portions using a syringe) a total of 245 mL (24.5 mmol) of 1.0M BH_3-THF complex. After ca. 75% of the reagent had been added, the reaction mixture formed an unstirrable gel. The mixture was heated at reflux for 1 hr, allowed to cool, and diluted with 400 mL water to give a clear, yellow-brown solution. This quenched reaction mixture was extracted with ether and the ether extracts were washed with 5% aqueous $NaHCO_3$, saturated aqueous NaCl, dried (Na_2SO_4) and concentrated in vacuo to give 31.3 g crude 14 (84% yield, ca. 100% conversion). From the bicarbonate wash was recovered ca. 8 g dihydroferulic acid.

Vacuum distillation of 18.9 g of crude 14 yielded 13.2 g of purified 14: bp 178-180°C (1 mm Hg); IR (neat) cm^{-1} 3400 (OH) and 1520, 1600 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.82 (m, 2, CH_2CH_2OH), 2.59 (t, J = 7 Hz, 2, $ArCH_2$), 3.62 (t, J = 7 Hz, 2, CH_2OH), 3.76 (s, 3, $ArOCH_3$), and 6.5-6.9 (multiplets, 3, aryl).

The sodium salt of 14 was prepared by dissolving 5.6 g (30.6 mmol) of the phenol in 30.6 mL of 1.00N aqueous NaOH; the water was removed *in vacuo*. Two 50 mL portions of 1,2-dichloroethane were added and evaporated *in vacuo* to remove residual moisture; the vacuum was always purged with nitrogen, and the contents chilled to ca. 0°C between 1,2-dichloroethane additions. The residual sodium salt of 14 was a fluffy off-white solid which was desiccated for 24 hr over fresh P_2O_5 before its subsequent use.

4-Hydroxy-3-methoxy-β-(2-methoxy-4-[γ-hydroxypropyl]phenoxy)-acetophenone (15) - The dimer 15 was prepared by the general coupling technique of Hosoya, *et al.*,[13] as modified by Dimmel, *et al.*[17] Three equivalents of the sodium salt of 14 (30.6 mmol) were dissolved in 25 mL dry DMF (dried over molecular sieves) and stirred under nitrogen while 2.5 g (10.2 mmol) of β-bromoacetoguaiacone (13) in 25 mL DMF was added dropwise over 1 hr, while the reaction mixture was kept at 50°C. Stirring was continued for 1 hr after complete addition of 13; the mixture was then diluted with 250 mL water, acidified with HCl, and extracted with $CHCl_3$. The organic layer was washed with large amounts of water to remove excess DMF. The chloroform layer was concentrated *in vacuo*; the residual syrup was diluted with two 50 mL portions of xylenes and concentrated under high vacuum (ca. 1 mm Hg) leaving 6.8 g of organic material.

A portion of the above material (4.1 g), which was a mixture of product 15 and excess 14, was subjected to column chromatography (silica gel 60, hexane/acetone 1:1) to give a 2.6 g portion of 15, as a syrup. The syrup was crystallized from *i*-PrOH to give 1.3 g (61%) of 15 as light-yellow needles: mp 94.5-96.0°C; IR (mull) cm^{-1} 3400 (OH), 1665 (C=O), and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ

1.65 (broad s, 1, CH_2OH), 1.84 (m, 2, CH_2CH_2OH), 2.64 (t, J = 7 Hz, 2, $ArCH_2$), 3.66 (t, J = 6.5 Hz, 2, CH_2OH), 3.85, 3.92 (2 s, 6, $ArOCH_3$), 5.25 (s, 2, CH_2OAr), 6.36 (broad s, 1, ArOH), 6.6-7.0 (m, 4, aryl), and 7.58 (m, 2, aryl); ^{13}C-NMR ($CDCl_3$) ppm 31.7 (t, CH_2CH_2OH), 34.2 (t, $ArCH_2$), 56.1 (q, two $ArOCH_3$), 62.1 (t, CH_2OH), 72.6 (t, CH_2OAr), 110.6, 113.2, 114.1, 115.6, 120.4, 123.3 (all d, aryl CH), 127.6, 136.2, 145.9, 146.8, 149.7, 151.1 (all s, aryl C), and 193.2 (s, C=O); MS (DIP) m/e (%) 346 (26, M^+), 151 (100), and 137 (14).

4-Hydroxy-3-methoxy-β-(2-methoxy-4-[δ-trityloxypropyl]phenoxy) acetophenone (15-Tr) - Tritylpyridinium tetrafluoroborate reagent (TPFB) was prepared according to the method of Hanessian and Straub.[16] Into 25 mL of spectroscopic grade acetonitrile was dissolved 0.5 g (1.44 mol) of 15 and 0.9 g (1.5 equiv.) of TPFB. The solution was kept at 55-60°C and after 24 hr the reaction progress seemed sluggish (by tlc); two more 0.5 g portions of TPFB were added on successive days. After 5 days the entire reaction mixture was evaporated to dryness in vacuo and the solid residue was extracted with $CHCl_2$. The chloroform extracts were washed with water, dried (Na_2SO_4), and concentrated in vacuo to give an oily residue which was visually contaminated with trityl alcohol crystals. This crude product was chromatographed on alumina (Alumin-AR CC-10, CH_2Cl_2/methanol 40:1 to 20:1) to give a 0.3 g fraction (35%) of 15-Tr as a colorless oil: IR (neat) cm^{-1} 1690 (C=O), and 1595 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.87 (m, 2, CH_2CH_2OTr), 2.66 (t, J = 7 Hz, 2, $ArCH_2$), 3.10 (t, J = 6 Hz, 2, CH_2OTr), 3.80, 3.90 (2 s, 6, $ArOCH_3$), 5.21 (s, 2, CH_2OAr), 6.5-7.0 (m, 2, aryl), and 7.2-7.6 (m, 19, aryl).

2-(2-Methoxyphenoxyl)-1-(3-methoxy-4-hydroxyphenyl)-4-penten-1-one (19) - The following alkylation procedure[17] employed oven-dried glassware, freshly distilled anhydrous solvents, and nitrogen atmospheres. To 150 mL of ice-cooled THF was added 224 mL (0.347 mol) of 1.55M n-BuLi in hexane and 35.1 g of diisopropylamine. After stirring 15 min, the solution was cooled to -70°C

and 25.0 g (86.7 mmol) of 3-methoxy-4-hydroxy-β-(2'-methoxyphenoxy)acetophenone (16)[17] dissolved in 150 mL THF was added dropwise. The stirred mixture was then allowed to warm to room temperature for 1 hr, followed by cooling again to -70°C; to this mixture, 42.0 g (0.347 mol) of allyl bromide (dissolved in 100 mL THF) was added dropwise. After complete addition of the allyl bromide, the mixture was allowed to warm to room temperature and stirred for several hours. The reaction mixture was quenched by the addition of 0.5N H_2SO_4. The organic layer was separated, and the aqueous layer was extracted with ether. The combined THF/ether extracts were extracted with 1N NaOH; these NaOH extracts were acidified and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo to give ca. 30 g of a brown oil. The oil was chromatographed (silica gel 60, $CHCl_3$/EtOAc 6:1) to give 19.4 g (68.1%) of 19 as a gold oil: IR (neat) cm^{-1} 3400 (OH), 3190, and 1635 ($CH=CH_2$), 1670 (C=O), and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ 2.81 (t, J = 7 Hz [with further fine splitting], 2, $CH_2CH=$), 3.77, 3.87 (2 s, 6, $ArOCH_3$), 5.0-5.4 (m, 3, CHOAr and $=CH_2$), 5.8-6.2 (m, 1, -CH=), 6.39 (s, 1, OH), 6.85 (m, 5, aryl), and 7.70 (m, 2, aryl); ^{13}C-NMR ($CDCl_3$) ppm 37.7 (t, $CH_2CH=$), 55.6 (q, $ArOCH_3$), 81.4 (d, CHOAr), 113.9 (t, $=CH_2$), 132.7 (d, $CH=CH_2$), 110.7, 112.4, 116.1, 117.6, 120.5, 122.1, 123.8 (all d, aryl CH), 126.9, 146.5, 146.8, 149.5, 150.8 (all s, aryl C), and 196.1 (s, C=O); MS (DIP) m/e (%) 328 (24, M^+), 205 (10), 177 (15), 151 (100), 123 (15) and 77 (11),

2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-4-penten-1-ol (22) - Into 300 mL of absolute EtOH was dissolved 20.0 g (60.9 mmol) of 19. Six equivalents (13.8 g) of $NaBH_4$ were quickly dissolved in 150 mL water/50 mL EtOH and added dropwise to the substrate solution. After 1 hr, the solution was quenched by the dropwise addition of 3N HCl, diluted with more water, and extracted with CH_2Cl_2. The organic extracts were dried (Na_2SO_4) and concentrated in vacuo to leave 20.4 g of an oil. The crude

product was chromatographed (silica gel 60, CH_2Cl_2/EtOAc 20:1 to 5:1) to give a major fraction of 13.0 g (64.7%) of **30**, as a colorless oil: IR (neat) cm^{-1} 3100 (OH), 1650 (C=C), no C=O absorbance, and 1600 (aryl); ^{1}H-NMR ($CDCl_3$) δ 2.0-2.2, 2.4-2.7 (2 m, 1 + 1, nonequiv $CH_2CH=CH_2$), 3.8-3.9 (broad signal, 1, OH), 3.87 (s, 6, $ArOCH_3$), 4.1-4.3 (m, 1, CHOAr), 4.80 (d, J = 3 Hz, 1, CHOH), 4.9-5.1 (m, 2, $=CH_2$), 5.74 (s, 1, ArOH), 5.7-6.0 (m, 1, -CH=), and 6.67-7.13 (m, 7, aryl); ^{13}C-NMR ($CDCl_3$) ppm 32.8 (t, $CH_2CH=$), 55.7 (q, two $ArOCH_3$), 72.8 (d, CHOH), 6.4 (d, CHOAr), 116.7 (t, $=CH_2$), 131.3 (d, $CH=CH_2$), 109.0, 112.0, 114.0, 119.0, 119.7, 121.1, 123.1 (all d, aryl CH), and 134.8, 144.6, 146.3, 146.9, 151.1 (all s, aryl C); MS (DIP) m/e (%) 330 (10, M^+), 206 (15), 178 (52), 177 (20), 153 (100), 124 (52), and 137 (19).

The chromatography fractions preceding the main component (**22**) collectively weighed 1.0 g and, based on NMR analysis, were mixtures of starting material **19** and product **22**. The fractions after the main component collectively weighed 3.0 g and were a mixture of two isomers of **22**. A small amount of the minor isomer was isolated: ^{1}H-NMR ($CDCl_3$) δ 2.1-2.4 (m, 2, $-CH_2CH=$), 3.84 and 3.88 (s, 3 + 3, $ArOCH_3$), 4.0-4.2 (m, 1, -CHOAr), 4.73 (d, 1, J = 7 Hz, -CHOH), 4.9-5.3 (m, 2, $=CH_2$), 5.7-6.1 (m, 1, -CH=), 5.76 (s, 1, ArOH) and 6.8-7.1 (m, 7, aryl); ^{13}C-NMR ($CDCl_3$) ppm 35.4 (t, $CH_2CH=$), 55.7 (q, $ArOCH_3$), 75.8 (d, CHOH), 86.5 (d, CHOAr), 117.5 (t, $=CH_2$) 133.5 (d, $CH=CH_2$), 109.7, 112.0, 114.2, 118.7, 120.3, 121.0, 122.7 (all d, aryl CH) and 131.7, 145.4, 146.5, 148.0, 150.4 (all s, aryl C).

2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-1,5-pentanediol (21) - All procedures, until workup, employed oven-dried glassware, freshly distilled anhydrous solvent, and nitrogen atmospheres. Into 100 mL of THF was dissolved 12.0 g (36.3 mmol) of **30**; the mixture was chilled in an ice bath and 600 mL (8.2 equiv) of 0.5M disiamylborane (DSB)[27] in THF was added to the solution over 1 hr. The mixture was kept at ca. 0°C for 3 hours, after which 130 mL water was added to decompose residual hydride.

The organoborane was oxidized *in situ* at room temperature by adding 200 mL of 3N NaOH, followed by the dropwise addition of 183 mL of 30% H_2O_2. The aqueous phase was saturated with K_2CO_3 and the THF layer was separated. The aqueous layer was then extracted with additional THF and the combined THF was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated under high vacuum (ca. 1 mm Hg) to leave 14.7 g of a crude yellow oil. The crude product was subjected to three successive column chromatographies (silica gel 60, CH_2Cl_2/MeOH 50:1 to 20:1) to give 11.4 g of a colorless oil which crystallized upon standing for several days; the product was recrystallized from benzene to yield 8.1 g (64.3%) of compound 21: mp 108.5-109.0°C; IR (mull) cm^{-1} 3450, 3225 (OH), and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.5-2.1 (m, 5, CH_2CH_2 and OH), 3.55 (broadened t, J = 6 Hz, 3, CH_2OH and OH), 3.81, 3.82 (2 s, 6, $ArOCH_3$), 4.25 (m, 1, CHOAr), 4.80 (d, J = 3 Hz, 1, CHOH), 5.74 (s, 1, ArOH), and 6.7-7.1 (m, 7, aryl) [the ^{1}H-NMR assignments were verified with homonuclear decoupling experiments]; ^{13}C-NMR ppm ($CDCl_3$) 24.5, 29.3 (2 t, CH_2CH_2), 56.1 (s, 2, $ArOCH_3$), 62.8 (t, CH_2OH), 73.1 (d, CHOH), 86.4 (d, CHOAr), 109.5, 112.7, 114.2, 119.2, 119.4, 121.4, 123.1 (all d, aryl CH), and 132.0, 145.0, 146.6, 147.4, 151.4 (all s, aryl C); MS (DIP) m/e (%) 348 (14, M^+), 224 (16), 196 (27), 153 (68), 137 (15), 124 (75), and 71 (100).

Anal., calcd. for $C_{19}H_{24}O_6$ (%): C 65.50; H 6.94; O 27.55. Found: C 65.78; H 6.96; O 27.26 (by difference).

2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-5-triphenylmethoxy-1-pentanol (21-Tr) - Into 75 mL freshly distilled, anhydrous pyridine was dissolved 1.53 g (4.39 mmol) of 21 and 2.41 g (2 equiv.) of trityl chloride. The reaction mixture was maintained at ca. 50°C for 5 days, and then diluted with 75 mL water. The aqueous pyridine solution was extracted with toluene, which was in turn washed repeatedly with water (until the wash was neutral), washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated *in vacuo* to leave 4.7 g of an oil. The crude product

was chromatographed on alumina (AluminAR CC-10, CH_2Cl_2/MeOH, pure CH_2Cl_2 to 20:1) to give 2.17 g of a colorless oil, which was crystallized from warm MeOH to yield 1.67 g (64.5%) of 21-Tr: mp 109.5-111.0°C; IR (mull) cm^{-1} 3450, 3270 (OH) and 1600, 1580 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.4-2.1 (m, 4, CH_2CH_2), 3.04 (t, J = 6 Hz, 2, CH_2OTr), 3.66 (d, J = 3 Hz, 1, OH), 3.77, 3.84 (2 s, 6, $ArOCH_3$), 4.13 (m, 1, CHOAr), 4.76 (t, J = 3 Hz [d after D_2O wash], 1, CHOH), 5.65 (s, 1, ArOH), 6.6-7.0 (m, 7, aryl), and 7.0-7.4 (m, 15, trityl); ^{13}C-NMR ($CDCl_3$) ppm 24.2, 26.3 (2 s, CH_2CH_2), 55.8 (q, two $ArOCH_3$), 62.9 (t, CH_2OH), 72.6 (d, CHOH), 86.1 (s, CAr_3), 86.7 (d, CHOAr), 108.7, 111.9, 114.0, 118.8, 119.9, 121.3, 123.2 (all d, aryl CH), 126.6, 127.5, 128.4 (all d, trityl aryl CH), 144.0 (s, trityl aryl C), and 131.4, 144.5, 146.4, 146.8, 151.4 (all s, aryl C); MS (DIP) m/e (%) 244 (22), 243 (100, Tr^+), 223 (17), 165 (25), and 153 (36).

Anal., calcd. for $C_{38}H_{38}O_6$ (%): C 77.26; H 6.48; O 16.25. Found: C 76.87; H 6.54; O 16.59 (by difference).

5-Hydroxy-2-(2-methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-1-pentanone (20) - The DSB procedure described above was repeated with compound 19, using the following quantities: 4.8 g (14.6 mmol) of 19, 88 mL (3 equiv.) of 0.5M DSB, and the appropriate amounts of NaOH and H_2O_2 during the workup. The crude product, 5.5 g, was chromatographed (silica gel 60, CH_2Cl_2/MeOH 30:1 to 10:1) to yield 1.8 g (36%) of 20 as an oil: IR (neat) cm^{-1} 3400 (OH), 1670 (C=O), 1590 (aryl), and no C=C absorbances; ^{1}H-NMR (d_6-DMSO) δ 1.65, 1.89 (2 m, 4, CH_2CH_2), 3.46 (t, J = 6 Hz, 2, CH_2OH), 3.76, 3.93 (2 s, 6, $ArOCH_3$), 4.48 (broad s, 1, OH), 5.63 (t, J = 5 Hz, 1, CHOAr), 6.94 (m, 4, aryl), 7.62 (m, 2, aryl), and 10.15 (broad s, 1, ArOH); ^{13}C-NMR (d_6-DMSO) ppm 28.2, 29.7 (CH_2CH_2), 55.8 ($ArOCH_3$), 60.4 (CH_2OH), 80.3 (CHOAr), 112.3, 113.3, 115.0, 115.4, 120.5, 121.4, 123.1, 126.4, 147.1, 147.3, 149.4, 151.9 (aryl), and 195.5 (C=O).

Compound 21 (Alternate Preparation) - The $NaBH_4$ reduction procedure described above was repeated with compound 20, using the

following quantities: 2.9 g (8.4 mmol) of 20 and 1.9 g (6 equiv.) of $NaBH_4$. The crude product, 2.8 g, was chromatographed (silica gel 60, CH_2Cl_2/MeOH 50:1 to 30:1) to yield 1.4 g (48%) of 21 as an oil which was a mixture of diastereomers: IR (neat) cm^{-1} 3400 (OH), no C=O absorbance, and 1595 (aryl); ^{1}H-NMR ($CDCl_3$) 1.4-2.0 (m, 4, CH_2CH_2), 2.10 (s, 1, OH), 3.60 (t, J = 6 Hz, 2, CH_2OH), 3.83, 3.85 (2s, 6, $ArOCH_3$), 4.1-4.2 (m, 1, CHOAr), 4.74 (d, J = 8 Hz, 0.3, CHOH), 4.82 (d, J = 3 Hz, 0.7, CHOH), 5.29 (s, 1, OH), 5.77 (broad s, 1, ArOH), and 6.6-7.1 (m, 7, aryl); ^{13}C-NMR ($CDCl_3$) ppm 24.2, 29.1 (CH_2CH_2, major), 27.4, 28.1 (CH_2CH_2, minor), 55.7 (2 $ArOCH_3$), 62.5 (CH_2OH), 72.6 (CHOH, major), 76.1 (CHOH, minor), 86.5 (CHOAr), 108.8, 112.0, 114.0, 118.7, 119.1, 121.2, 123.0 (aryl CH, major), 109.4, 117.8, 119.4, 120.7, 121.0, 122.4 (aryl CH, minor), 131.5, 144.5, 146.3, 146.7, 151.0 (aryl C, major), and 131.8, 145.2, 148.2, 148.1, 150.0 (aryl C, minor); MS (DIP) m/e (%) 348 (2, M^+), 224 (10), 196 (16), 153 (46), 137 (13), 124 (51), and 71 (100). The major isomer here matches the one obtained by reduction of 22, except the ^{13}C-NMR signals here are all lower by roughly 0.3-0.5 ppm (indicative of an instrument instability problem).

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REFERENCES

1. Sarkanen, K. V., and Ludwig, C. H., ed., Lignins - Occurrence, Formation, Structure, and Reactions, Wiley Interscience, New York, Chapter 17, p. 695 (1971).
2. Gierer, J., Svensk Papperstidn., 73, 571 (1970).
3. Gierer, J. and Noren, I., Holzforschung, 34, 197 (1980).
4. Gierer, J., Ljunggren, S.; Ljungquist, P., and Noren, I., Svensk Papperstidn., 83, 75 (1980).
5. Apfeld, P. B. and Dimmel, D. R., J. Wood Chem. Technol., paper to follow.

6. Helferich, B., Advan. Carbohyd. Chem., 3, 80 (1948).

7. Kawana, M. and Emoto, S., Tetrahedron Lett., 13, 4855 (1972).

8. Hodge, P. and Sherrington, D. C., ed. Polymer-Supported Reactions in Organic Chemistry, Wiley-Interscience, New York, Chapters 6 and 8, pp. 293 and 407 (1980).

9. Fyles, T. M. and Lesnoff, C. C., Can. J. Chem., 54, 935 (1976).

10. Frechet, J. M. J. and Nuyens, L. J., Can. J. Chem., 54, 926 (1976).

11. Dimmel, D. R. and Schuller, L., J. Wood Chem. Technol., 6, 345 (1986).

12. Panetta, J. A. and Rapoport, H., J. Org. Chem., 47, 946 (1982).

13. Hosoya, S., Kanazawa, K., Kaneko, H., and Nakano, J., J. Japan Wood Res. Soc., 26, 118 (1980).

14. Miksche, G. E., Acta Chem. Scand., 27, 1355 (1973).

15. Gierer, J. and Ljunggren, S., Svensk Papperstidn., 82, 71 (1979).

16. Hanessian, S. and Staub, A. P. A., Methods Carb. Chem., VII, 63 (1976).

17. Dimmel, D. R. and Shepard, D., J. Wood Chem. Technol., 2, 297 (1982).

18. March, J. Advanced Organic Chemistry: Reactions, Mechanisms, and Structures, 2nd Ed., McGraw-Hill, New York, Chapter 10, p. 316 (1977).

19. Zweifel, G. and Brown, H. C., Org. Reactions, 13, 1 (1963).

20. Cram, D. J. and Abd Elhafez, F. A., J. Org. Chem., 74, 5828 (1952).

21. Eliel, E. L., Asymmetric Synthesis II(A), Academic Press, New York, J. D. Morrison, ed., (1983), p. 125.

22. Ibid., Chapter 3, p. 106.

23. Fieser, L. F. and Fieser, M., Reagents for Organic Synthesis. John Wiley and Sons, New York, 1967, 1254.

24. Dimmel, D. R., Schuller, L., and Apfeld, P. B., J. Wood Chem. Technol., 7, 97 (1987).

25. Stetter, H. and Uerdingen, W., Synthesis, 207 (1973).

26. CRC Handbook of Chemistry and Physics, 56th Ed., p. C-450 (1975/76).

27. Aldrich Technical Information Bulletin No. Al-109.